Awake craniotomy versus general anesthesia for managing eloquent cortex low-grade gliomas

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ABSTRACT

الأهداف: مقارنة تخدير أورام الجليوما المخية بطيئة النمو والتي تصيب القشرة السائدة تخديرا موضعيا و عمل الشق الجمجمى والمريض مستيقظ مع إعطاءه بعض الأدوية المهدئة ضد التخدير الكلي التقليدي.

الطريقة: شملت هذه الدراسة المتابعة 40 مريض ضمن تصنيف الجمعية الأمريكية للتخدير(ASA) العمر (55-23) عام يعانون من أورام الجليوما بطيئة النمو وقريبة من القشرة السائدة. أجريت هذه الدراسة بعمليات جراحة الأعصاب – مستشفى القصر العيني مابين الفترة يناير2007 حتى نوفمبر 2008. ضمت المجموعة الأولى 20 مريضا خدروا تخديرا كليا بالطريقة التقليدية، بينما تم تخدير المجموعة الثانية تخديرا موضعيا لأعصاب جلد الرأس مع إعطاء البروبوفول والفنتانيل عن طريق الحقن الوريدي.

النتائج: أكمل 40 مريضا الدراسة. لم يحتاج أي مريض لمخدر كلي في المجموعة الثانية، حدث توتر شديد في حالتين، كان تأثير المهدئ قوي لدى 5 حالات، ولم يتعرض أي مريض لغثيان أو قئ أثناء الجراحة. في مجموعة التخدير الكلى (GA) تعرض 4 مريض لحالات غثيان أو قئ بعد الجراحة مقابل 1 في المجموعة الثانية (p=0.039). في المجموعة الثانية، لم تحدث مضاعفات للكلام أو الحركة بعد الجراحة مباشرة في90% من مجموعة 2 مقابل 40% في مجموعة GA (الفارق مهم إحصائيا). بعد 6 أشهر كانت النتائج علي الترتيب (90%) و 60% (الفارق غير مهم إحصائيا). تم استئصال الورم كليا في 10 حالات مجموعة GA مقابل 8 مجموعة 2 ولكن الفارق غير مهم إحصائيا.

خاتمة: تبين أن جراحات الشق الجمجمى تحت التخدير الموضعي سهلة وغير مكلفة وتتيح استئصال الورم مع إمكانية المحافظة علي وظائف المخ مقارنة مع التخدير الكلي.

Objectives: To compare awake craniotomy using conscious sedation technique versus conventional general anesthesia (GA) for excision of low-grade glioma encroaching on eloquent brain.

Methods: This prospective study included 40 patients ASA classification 1 and 2, aged 23-55 years, harboring low-grade glioma encroaching on eloquent brain. The study was carried out in the Neurosurgical Theatre in Kasr El-Aini Hospital, Cairo, Egypt, from January 2007 to November 2008. Twenty patients (group 1) received GA with endotracheal intubation and controlled ventilation. In group 2, awake craniotomy was carried out using local anesthetic infiltration, and intravenous injection of propofol and fentanyl.

Results: Forty patients completed the study. In the awake group, none of the patients received GA, 2 patients developed intraoperative agitation, 5 patients were over-sedated, and none of the awake patients developed intraoperative nausea or vomiting. Four patients in the GA group developed post-operative nausea and vomiting compared to one patient in the awake group, and this difference was statistically significant (p=0.039). The neurological outcome regarding motor power and/or speech was found better or with no fresh deficits, immediately postoperative in 90% of the awake group patients. This is compared to 40% in the GA group. The difference was statistically significant. At 6 months follow up, the results were 90% and 60%, but the difference was not statistically significant. Gross total tumor resection was achieved in 10 cases of the GA group versus 8 in the awake group; however, the difference was not statistically significant.

Conclusion: Compared to GA, awake craniotomy is a relatively simple non-expensive procedure that allows tumor removal guided by physiology rather than anatomy.

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Radical tumor removal remains the main challenge in oncological surgery. In most cases, the larger the resection the lower the risk of recurrence of the lesion and the higher the chance of the patient's survival. However, depending on the location of the malignancy, an extensive tissue excision may favor the occurrence of an unpredictable degree of functional loss.[1] This is true particularly in low grade glioma, which may be discovered in asymptomatic patients, where the neurological sequelae due to tumor excision may cause severe disability compromising the patient's social life.[2] With evolution of general anesthesia (GA), optimal working conditions for neurosurgery were achieved in the form of adequate control of vital parameters, neurological function, and intracranial pressure (ICP). Nevertheless, intraoperative monitoring of functional lesions of the CNS was severely inhibited by GA: some higher cortical brain functions (for example, speech) could not be monitored during surgery.[3] Awake craniotomy dates back to the second half of the 19th century, and at that time, the indication was epilepsy surgery performed under local anesthesia. Subsequently, this surgical practice has been extended also to the resection of tumors involving the functional cortex and finally, in more recent years, the indications have further extended to include the removal of supratentorial tumors, regardless of the involvement of the cortex.[4] Apart from tumor anatomical location, mandatory prerequisites for awake craniotomy are a fully cooperative patient and optimal collaboration between anesthesia and neurosurgical staff, to realize what is defined as function controlled neurosurgery.[5] Multiple and competing goals are required during awake craniotomy. Carefully monitoring and altering depth of anesthesia throughout the procedure is mandatory to facilitate opening and closing of the bone flap at craniotomy, with a return to full consciousness during cortical mapping. A smooth transition between these states must be achieved, as well as adequate ventilation and patient comfort, immobility, and cooperation. In common with more conventional procedures, it is during the transition periods between anesthesia, sedation, and consciousness that the risk of complications, morbidity, and mortality is greatest.[6] This study aims at comparing the technique of awake conscious sedation with local anesthesia versus the conventional technique of GA for excision of low-grade glioma regarding anesthetic and respiratory complications, peri-operative events, and neurological outcome. It is our goal to assess the safety and tolerance of awake craniotomy in solving the problem of low-grade glioma in a setting where modern and expensive technology like functional MRI, intraoperative MRI, intraoperative cortical mapping and electrophysiology monitoring are not available.

Methods. After the approval of the Ethical and Scientific Committee of the Anesthesia Department of Cairo University, and obtaining informed written consent from each patient, 40 patients were included in this study. It was carried out in the Neurosurgical Theatre in Kasr El-Aini Hospital, Cairo, Egypt from January 2007 to November 2008. Inclusion criteria in this study included patients aged between 20-55 years, American Society of Anesthesiologists grade 1 and 2, undergoing resection of low-grade glioma encroaching on an eloquent brain area. The eloquent cortex areas were defined as the motor areas (bilateral precentral gyrus) and speech areas (left frontal operculum and angular gyrus, superior temporal gyrus). Preoperative localization of the glioma was carried out by both CT and MRI with contrast. Functional MRI is of great benefit when available, but unfortunately it was not available in our hospital. Exclusion criteria for awake craniotomy included patients with confusion, communication difficulties, extreme anxiety, morbid obesity, chronic obstructive pulmonary disease, complicated airway, end organ affection in the form of hepatic, cardiovascular, or renal impairment. Patients with a history of allergy to local anesthetics or drugs used in the study were also excluded. Surgeries carried out in a position other than the supine position, or that lasted more than 4 hours were excluded. Patients were divided into 2 groups to receive either awake anesthesia with conscious sedation, or conventional GA; each group included 20 patients.

Anesthetic technique. Group 1 - general anesthesia (20 patients). On arrival to the theater a 20G IV cannula was inserted on the dorsum of the hand. Extra large bore venous access was inserted after induction. No premedication was given. A radial artery 20G cannula was inserted under local anesthesia in the non-dominant hand after negative Allen's test. Full monitoring was be applied in the form of 5-lead ECG, invasive blood pressure, core temperature monitoring by a nasopharyngeal probe, capnography, pulse oximetry, peripheral nerve stimulator, and indwelling urinary catheter. Intravenous induction of anesthesia was achieved with propofol (1.5-2 mg/kg), fentanyl (2-3 μg/kg), atracurium (0.5 mg/kg as a bolus dose over 30 seconds) and lidocaine (1.5 mg/kg 90 seconds before endotracheal intubation). Anesthesia was maintained with isoflurane (1-2% concentration) in N_2O:O_2 50% and atracurium infusion at a rate of 0.5 mg/kg/h to maintain muscle relaxation. Mechanical ventilation was instituted with hyperventilation to keep arterial carbon dioxide tension ($PaCO_2$) around 30 mm Hg. Patients received mannitol 20% 0.5 g/kg over 20 minutes, dexamethasone (8 mg), and phenytoin 5 mg/kg, crystalloid administration was limited to 3 ml/kg/h of normal saline with replacement of blood

losses by an equal volume of blood or colloids (Haes-Steril® Fresenius Kapi, Bad Homburg, Germany). At the end of surgery, the inhalational anesthetic was discontinued and muscle relaxation reversed with neostigmine (0.05 mg/kg) and atropine (0.02 mg/kg) before the patient was extubated.

Group 2 - awake craniotomy (20 patients). The operative team including anesthesiologists and neurosurgeons involved with the procedure visited these patients one day prior to surgery. An explanation of the procedure sequence, and the situations during which pain or discomfort might be experienced, were given to reassure them. Patients fasted since midnight and the following drugs were administered IV in the preanesthesia room: clonidine (4 µg/kg), ranitidine (50 mg), and metoclopramide 10 mg, dexamethasone 8 mg, ranitidine 50 mg, phenytoin 5 mg/kg, diclofenac, and paracetamol (1 gm) intravenously half an hour before surgery. Benzodiazepine and anticholinergics were avoided. Preparation in the operating room involved making the patient as comfortable as possible. The operating room temperature was kept warm and in some cases, a forced air-warming device was used. Once patients arrived in the operating room, an intravenous cannula was inserted, the patient was monitored with ECG, non-invasive blood pressure, pulse oximetry (SpO2), urine catheter was not routine and inserted if needed. Oxygen was started via a nasal cannula (2-4 liter/minute). A bolus dose of propofol (50-100 mg), and 50 ug fentanyl were given to insert an arterial cannula in one of the radial arteries and then scalp nerve block was performed bilaterally in all patients by a mixture of 0.25% bupivacaine and 1% lignocaine with 1:200,000 adrenaline (2-3 ml at each infiltration site). An anesthesiologist was dedicated to observation and maintenance of a patent airway and proper ventilation and oxygenation during injection of the local anesthetic. The nerves infiltrated were supratrochlear and supraorbital, auriculotemporal, zygomaticotemporal, greater and lesser occipital, and great auricular. Also local anesthetic infiltration was applied at the site of skin incision and the sites of pin insertion. In most cases, Mayfield frame was used to fix the head (**Figure 1a**), in others a horseshoe holder was used. Dural block was carried out intraoperatively after raising a bone flap and exposing the dura. Lidocaine 1% was instilled around the trunk running with the middle meningeal artery and field block around the edge of the craniotomy was performed. A total dose of local anesthetics was carefully calculated to avoid exceeding permissible limit. After awakening from the bolus dose of propofol, the patient was put in the most comfortable position, which also allows for emergency intubation if needed.

Maintenance of anesthesia. After recovery from the initial bolus dose of propofol, a conscious sedation technique using propofol (1-2 mg/kg/h) and fentanyl (0.5 µg/kg/h) using 2 separate syringe pumps in 2 separate cannula. Fluid management was similar to the former group.

Surgical technique for awake craniotomy. In the supine position (for all patients) local anesthetic infiltration was carried out as prescribed. Craniotomy should be as small as possible, rapidly carried out, with the patient awake, except in the temporal region where it is too painful and the patient should be well sedated (**Figures 1b & 1c**). The most superficial part of the lesion was entered. Continuous monitoring with resection was performed by observing the patient for speech and motor function. Cortical mapping was not used in our series. The neurosurgical assistant tested the patient for naming, counting, repetition as well as motor activity by moving his limb or grasping (**Figures 2a & b**). Once we observed a delay in performing function, surgery was stopped temporarily. If the deficit persisted, surgery was terminated even if residual tumor was still seen. In

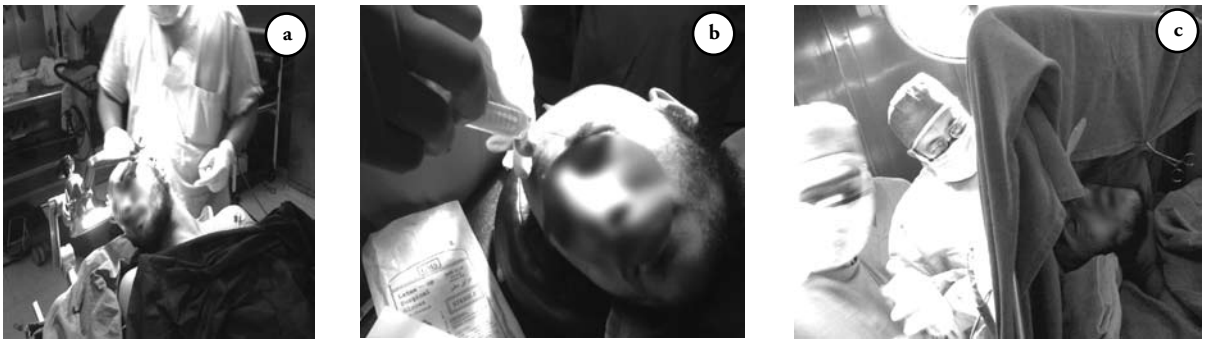

Figure 1- Awake craniotomy technique showing **a)** Mayfield fixation. **b)** Local anesthetic infiltration of supraorbital nerves. **c)** Craniotomy carried out with patient sedated.

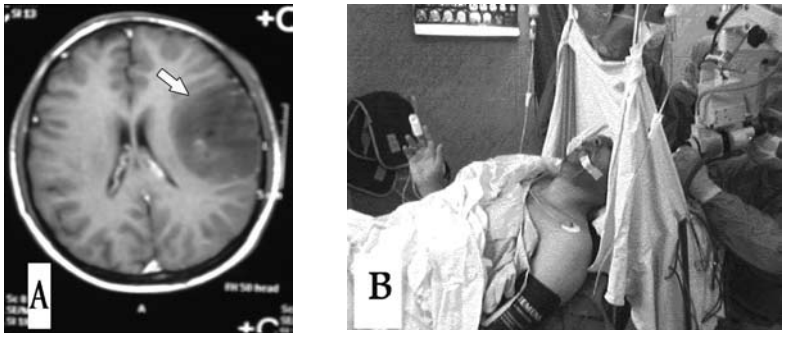

Figure 2 - Patient with glioma over the left motor area. **A**) MRI T1. **B**) He is asked to raise his right hand during tumor removal.

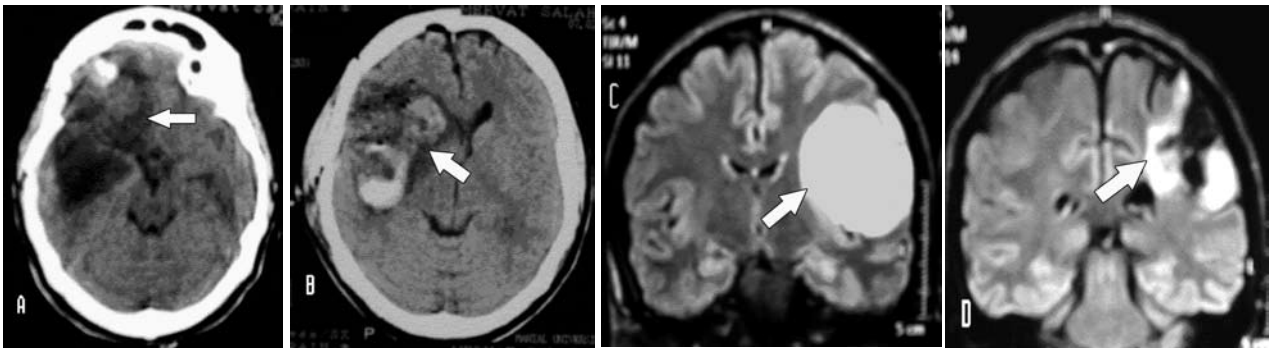

Figure 3 - Patient CT & MRI before and after awake excision: **A**) Preoperative CT. **B**) Immediate postoperative CT. **C**) Preoperative MRI. **D**) MRI 2 months postoperative showing extent of resection.

case seizures developed, they usually lasted less than 30 seconds and were aborted by cold saline application to the cortex, if this failed benzodiazepine was given and the procedure aborted. Patient evaluation was continued immediately postoperatively, and at regular visits every 2 weeks for 6 months. A CT scan was carried out on the second day after surgery, while MRI was carried out after 2 months to evaluate extent of resection (**Figures 3a-d**).

Data collection. 1. Hemodynamic data. Systolic, diastolic, and mean arterial pressures, together with heart rate were recorded at baseline (before administration of general or local anesthetics), every 15 minutes intraoperatively, and every 30 minutes postoperatively for 2 hours. Hypertension was defined as systolic blood pressure more than 150 mm Hg, hypotension was defined as systolic blood pressure <90 mm Hg, tachycardia was defined as heart rate more than 100 bpm, and bradycardia was defined as heart rate <45 bpm.[2,7] The proportion of cases with hemodynamic complications was noted. 2. Anaesthetic data. Pain, agitation, oversedation, shift to GA. 3. Airway and ventilation data. Airway/ventilation complications in awake cases were defined as apnea >30 seconds or placement of an oral or nasal airway to permit unobstructed breathing and/or adequate ventilation.[8] Airway/ventilation complications in GA cases were defined as difficulty (>3 attempts by more than 2 anesthesia care providers) or inability to insert an oral endotracheal tube, or difficulty with ventilation once the patient was intubated.[9] In both awake and GA, moderate oxyhemoglobin desaturation was defined as SpO_2 91-95% and severe oxyhemoglobin desaturation was defined as Spo_2 ≤90%. The proportion of cases with desaturation events was noted.[7,9] Arterial blood gas analysis (pH, PaO_2, $PaCO_2$, HCO_3^-) were performed at baseline, at skin incision, at dural incision, and after extubation. 4. Neuro-oncological data. Intracranial pressure as assessed by the surgeon (tense or not) prior to opening the dura, intraoperative seizures, bleeding, gross tumor resection, and new intra or postoperative neurologic deficits. 5. Other complications. Nausea without vomiting, nausea with vomiting,[10] bleeding, local anesthetic toxicity, pulmonary aspiration, air embolism,[11] and death. 6. Need for ICU admission.

Numerical data were described as mean+standard deviation. Two-tailed unpaired Student's t-tests were

used for comparison between normally distributed groups. Nominal data were described as percentage and range. They were compared using 2 test or Fischer's exact test as appropriate. A *p*-value <0.05 was considered statistically significant. The SPSS (Statistical Package for Social Sciences for Windows version 10.0 Chicago, IL, USA) was used for all statistical analysis.

Results. Forty patients completed the study. The demographic data of patients in the 2 groups are comparable (**Table 1**). None of the patients in the awake group received GA (**Table 2**). Two patients developed intraoperative agitation that was controlled by an extra-sedative dose, one of them needed urinary catheterization. In the awake group, 5 patients were over-sedated and required a decrease in the rate of propofol infusion, and oropharyngeal airway to overcome airway obstruction. Fourteen patients experienced intraoperative pain, which was severe in 2 cases only. Mild pain was controlled by IV 25 ug fentanyl, while severe pain required the stopping of surgery and administration of fentanyl, local infiltration, and an extra dose of propofol until the pain was controlled. None of the awake patients developed intraoperative nausea or vomiting, while postoperatively, one patient suffered from nausea and vomiting. In the GA group 4 cases developed PONV. Two patients in the awake group developed intraoperative focal seizures. None of the patients had manifestations of local anesthetic toxicity. Four patients in the awake group had subjective increased intracranial tension (tense brain) as compared to 6 patents in the GA group (**Table 3**). The difference was not statistically significant (*p*=0.46). Gross total tumor resection (GTR) was achieved in 10 cases of the GA group, versus 8 in the awake group. However, the difference was not statistically significant. Postoperative ICU admission was higher in patients in the GA group than in patients in the awake group: 14 in the GA group (5 seizures, 4 brain edema, 3 delayed recovery, and 2 agitation) and 2 in the awake group (one seizure, one brain edema) (**Table 3**). The difference was statistically significant (*p*=0.0004). The mean duration of hospital stay was 3.8 ± 4.15 days in the awake group, and 8.15 ± 6.5 days in the GA group; the difference was statistically significant

Table 1 - Demographic data and clinical characteristics of patients (mean ± SD).

Characteristics	Awake group (n=20)	GA group (n=20)	*P*-value
Age (years)	49.0 ± 7.44	50.9 ± 5.59	0.24
Weight (Kg)	73.5 ± 16.63	79.3 ± 21.13	0.36
Height (cm)	162.5 ± 15.05	168.3 ± 9.86	0.19
BSA (m^2)	1.88 ± 0.20	1.97 ± 0.22	0.42
Male/female	15/5	13/7	0.32
Duration of surgery (min)	173 ± 13	167 ± 15	0.27

GA - general anesthetic, BSA - body surface area

Table 2 - Perioperative events of patients in the awake group.

Events	Yes n (%)	No
Shift to general anesthesia	0 (0)	20
Intraoperative agitation	2 (10)	18
Over-sedation	5 (25)	15
Airway obstruction (apnea >30sec) ↑$paCO_2$,↓SaO_2	3 (15)	17
Intraoperative pain		
Severe pain*	2 (10)	18
Mild pain**	14 (70)	6
Intraoperative nausea & vomiting	0 (0)	20
Intraoperative seizures	2 (10)	18
Local anaesthetic toxicity	0 (0)	20

*requiring stoppage of surgery and needed more than one drug
**requiring only one drug, such as fentanyl, or nonsteroidal injection
$paCO_2$ - arterial carbon dioxide tension, SaO_2 - oxygen saturation

Table 3 - Incidence of events in patients in both groups.

Events	Awake group (n=20)	GA group (n=20)	*P*-value
Tense brain	4	6	0.46
Intra-operative bleeding (ml; mean)	293	276	0.15
Gross total resection (GTR)	8	10	0.50
Postoperative ICU admission	2	14	0.0004
Mean hospital stay (days)	3.8 ± 4.15	8.15 ± 6.5	0.05
Site of glioma			0.248
Motor area	12	13	
Speech area	6	6	
Motor & speech	2	1	

ICU - intensive care unit

Table 4 - Neurological outcome.

Outcome	Awake group (n=20)	GA group (n=20)	*P*-value
	n (%)		
Immediate postop			
Same-improved	18 (90)	8 (40)	0.0006
Worse	2 (10)	12 (60)	
At 6 months follow up			
Same-improved	18 (90)	12 (60)	0.431
Worse	1 (5)	6 (30)	
Lost during follow up	1 (5)	2 (10)	

(p=0.05). The neurological outcome regarding motor power and/or speech was found better or with no fresh deficits, immediately postoperative in 90% of the awake group compared with 40% in the GA group, the difference was statistically significant (p=0.0006). At 6 months follow up, the results were 90% in the awake group and 60% in the GA group, and this was not statistically significant (**Table 4**).

Discussion. This study was carried out on 40 patients undergoing elective craniotomy to remove a low-grade glioma encroaching on eloquent areas of the brain to compare between 2 anesthetic techniques: awake anesthesia using conscious sedation versus conventional GA. Low-grade glioma patients, diagnosed by CT and MRI, have a better chance for both survival and GTR with less postoperative deficits as compared to glioblastoma patients.[12,13] Therefore, we selected those patients for awake craniotomy to gain the advantage of total or near total tumor resection with preservation of function. Exclusion criteria for awake craniotomy included patients with confusion, communication difficulties, extreme anxiety, morbid obesity, COPD, complicated airway, end organ affection in the form of hepatic, cardiovascular, or renal impairment. Patients with history of allergy to the local anesthetics or drugs used in the study were also excluded. Surgeries carried out in a position other than supine, or lasting more than 4 hours were excluded.

In this study, ICP was assessed subjectively by the surgeon, tense brain was found in 4 cases (20%), in the awake group with no significant difference to the GA group. The tense brain in the awake group did not interfere with the surgical procedure, we asked the patients to voluntary hyperventilate and head repositioning was carried out (more head elevation and decreasing head rotation), which was effective in reducing ICP in 3 cases, in the fourth case the tense brain was due to local effect by the tumor. These results coincide with results of Sinha et al,[10] who found that 14.2% of awake patients had "tight brain", on the other hand, Skucas et al,[14] found brain swelling only in 2 cases of 323 cases undergoing awake craniotomy. Other studies reported an incidence of tight brain of 1.4%[15,16] and 0.6%.[8] As mentioned by many authors; Zorzi et al[17] concluded that brain swelling was never a problem in awake craniotomy. During awake craniotomy, airway care represents a major challenge. Respiratory complications are the most feared during an unprotected airway sedation technique. Respiratory complications may occur as a consequence of oversedation, hypoventilation caused by anesthesia, and may be

accompanied by airway obstruction, hypoxemia, desaturation, and hypercarbia. Hypercarbia affects cerebral blood flow and ICP. It is difficult to accurately monitor expired carbon dioxide levels in sedated spontaneously breathing patients without airway instrumentation.[18] Simple measures to limit the occurrence and impact of these adverse effects includes careful attention to airway maintenance and position, the use of airway adjuncts such as a nasopharyngeal or oropharyngeal airways, and the delivery of a high inspired oxygen fraction. The anesthesiologist should anticipate respiratory complications, whatever the technique of awake craniotomy, and have a plan of action and required equipment to deal with difficult airway management.[7] The incidence of over sedation in the awake group was 25% (5 cases), 3 of them developed airway obstruction and apnea (cessation of respiration >30 seconds), with hypercarbia. Management was carried out by reducing propofol infusion and insertion of an oropharyngeal airway for 3 minutes. Oxygen saturation decreased to 94% in the remaining 2 patients as apnea was very transient, although it was repeated. The incidence of airway obstruction in the study of Saltarini et al[9] was 0.5% (they considered airway obstruction that needed endotracheal intubation or insertion of laryngeal mask airway), while in the study of Skucas[14] it was 1.8%, and in Sarang's[7] study it was 7%. In the asleep awake asleep (AAA) technique with unsecured airways,[14] airway compromise during AAA requiring urgent or emergent securing of the airway was relatively rare and occurred only in obese patients. Only 3 of 332 AAA patients required airway control with an endotracheal tube or laryngeal mask airway (LMA). There were no negative sequelae to patients who had respiratory complications or hypercapnia in this study. The GA group had no significant respiratory complications other than a slowly leaking endotracheal tube cuff in one patient.

Another major challenge in awake patients is the development of seizures and its management. Focal seizures induced by surgical mapping are commonplace, occurring in 7-10% of patients in many reported series,[2] which coincides with our results (10% of cases). They are often self-limiting, require little in the way of active management, provided that the patient does not complain of significant distress. Sedative or anticonvulsant agents affect the ability of the patient to cooperate at the time when this is most vital. Gebhard et al,[19] described selective, peripheral nerve blockade for the control of particularly severe focal seizures, avoiding the administration of anticonvulsant agents. Primary generalized seizures present a different risk profile. Their incidence is reported at anywhere from 5-19%.[2,7,20] Their treatment is at first expectant, because definitive management has significant implications for the procedure. If seizures persist, anticonvulsant therapy may be initiated. The most common agents used to terminate seizure activity include benzodiazepines, such as midazolam, or diazepam, or barbiturate agents such as thiopental and, until recently, methohexital. The use of these agents when sedation is already in progress may induce anesthesia with loss of verbal contact with the patient, loss of airway tone, and reflexes, and apnea. In these circumstances, it may become necessary to intervene and secure the airway by endotracheal tube and initiate positive pressure ventilation. Although this is a safe practice, many of the advantages of awake craniotomy are lost in the process.[18] In our study, the incidence of intraoperative seizures was 10%. With this high incidence, it was focal and responded to cortical irrigation with cold ringer's lactate or gauze soaked with cold lidocaine 1% applied to the surface of the brain or small doses of propofol. Zorzi et al[17] reported intraoperative seizures in 11% of cases, it was 3% in the study of Skucas.[14] These variations are related to the presence of epilepsy before surgery or not, the level of anticonvulsant drugs, and the anesthetic drugs used. We applied gauze soaked with cold lidocaine 1% to the surface of the brain before dural opening for 2 minutes, we think this maneuver did not prevent convulsions, but it ameliorated it. In the GA group, convulsions occurred in 2 patients (10%) 2 hours postoperatively, in one of them it was generalized and terminated after IV injection of 100 mg thiopentone.

Prevention of nausea and vomiting is of paramount importance in a conscious sedation state. Fortunately, none of our patients either nauseated or vomited intraoperatively. However, 5% of patients had incidence of PONV. While in the GA group the incidence was 20%. This low incidence in awake patients could be attributed to the prophylactic administration of antiemetic and antacid preoperatively, the lower dose opioids used, and the antiemetic effect of propofol. The absence of intraoperative nausea and vomiting was encountered in the study of Sinha et al,[10] but with 19% PONV, and other authors reported an incidence of PONV as high as 50%.[21]

Severe pain during awake craniotomy is uncommon and if it occurs, it must be managed with a view to the potential effect of analgesic agents on the sedative level. Other institutes have reported success with non-sedative analgesics either prospectively or intra-operatively. Intra-operative discomfort can be prevented by simple analgesia with acetaminophen or non-steroidal anti-inflammatory drugs, which can be very effective when used in conjunction with skin infiltration with local anesthetic. Supplemental opioids (fentanyl; IV bolus, and more recently, remifentanil by infusion) may be unavoidable if analgesia remains inadequate. We used

fentanyl, given by IV bolus, in this study. Both opioids have an impact on sedation level and increase the risk of perioperative nausea and vomiting, which impairs the awake patient's ability to stay immobile.[6] We classified intraoperative pain into mild and severe. Mild pain was encountered in 70% of cases and needed minimal intervention in the form of 25 ug fentanyl, while severe pain was encountered in 10% and required the stopping of the procedure and administration of fentanyl (25 ug), a small dose of propofol (2-3 mg), and local of infiltration of lidocaine 1%. We found the most painful steps during awake craniotomy were: temporalis muscle dissection, bone drilling, and dural manipulation especially, the dura around the middle meningeal artery. Intraoperative agitation occurred in 2 patients in the awake group, one of them due to full bladder and a urinary catheter was inserted and in the other case, pain was the cause, and managed as in severe pain.

The most common hemodynamic problem encountered during awake craniotomy is hypertension.[2,7] At some institutes, accurate recording of beat-to-beat blood pressure via an arterial catheter is considered highly desirable, if not mandatory, for awake craniotomy procedures. The most common causes of intra-operative hypertension are inadequate sedation and analgesia. Tachycardia often accompanies hypertension in these circumstances. By contrast, hypertension associated with bradycardia may be a sign of raised ICP, with its associated risk of cerebral herniation and brain injury. Propofol, the most commonly used intravenous sedative, reduces systemic vascular resistance and may precipitate significant hypotension as a result. Hypertension, which is unrelated to sedative level or pain, may require specific antihypertensive therapy. There are limitations to the use of drugs commonly used intra-operatively for this purpose, because many have profound effects on cerebral vasomotor tone.[6] In our study, there was a statistically significant difference between the 2 groups regarding hypertension (**Figure** 4). The high incidence of hypertension in awake patients relative to GA could be attributed to the high incidence of pain and to the variation in the definition of hypertension (in our study BP >150 mm Hg was consider hypertension). In most cases, recognition of hypertension prompted initiation of the appropriate treatment of fentanyl, increasing the rate of propofol infusion, and nitrate infusion was needed only in one case. This hypertension had no negative sequelae to the patients' surgical procedure.

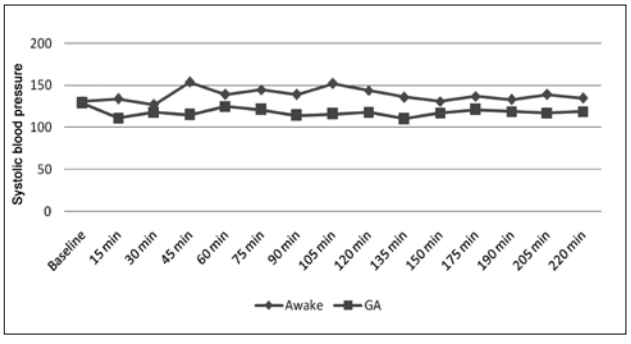

Figure 4 - Intraoperative systolic blood pressure in patients in both groups.

In this study, the incidence of neurological complications in the awake group was statistically less than in the GA group. Only 2 cases (10%) developed neurological deficits (aphasia in one case and hemiparesis in the other). In both cases, the deficit was observed intraoperatively, we stopped surgery and observed the patient, when no improvement occurred surgery was terminated at this stage in both cases. Within 4 weeks the aphasic patient improved completely. The other patient had G4 power preoperatively, which declined to G2 intraoperatively, immediate postoperative, and improved to G3 within 6 months. These results are lower than those of Skucas et al,[14] who had an incidence of 23.8% transient neurological deficits in their series with no reported incidence of permanent neurological deficit. They attributed this high incidence because they maximized surgical resection at the calculated risk of development of mild or acceptable neurological deficits. Taylor et al[22] reported an 8.5% incidence of transient, and 4.5% incidence of permanent neurological deficits. The GTR, was achieved in 40% of the awake group compared to 50% of the GA group. However, in terms of neurological deficits, 10% deficits occurred in the awake group, and 60% deficits occurred in the GA group. The GTR in the awake group was limited by development of intraoperative deficits or branches of the middle cerebral artery. These results reflect the improvement in the quality of life after surgery for low-grade glioma patients achieved with awake craniotomy compared to GA. Duffau et al[13] reported a series of 60 patients with various supratentorial brain lesions who underwent cortical mapping-guided resections, and GTR was achieved in 51% and permanent postoperative neurological deficits occurred in 5% in their series. Meyer et al[12] similarly had more than 90% resection of the MRI T2 WI defined tumor volume in 67% of patients with grade II gliomas (N=18) compared with only 11% neurological disability.

Several combinations of sedation, analgesia, and anesthetic techniques have been described in the medical literature. Whatever the strategy of anesthesia chosen, the final goals must allow the neurosurgeon to take advantage of the patient's cooperation and preserve general homeostasis. The anesthetic technique selected requires optimal analgesia during nociceptive stimulations; sedation, anxiolysis, immobility, and comfort during the

mapping and resection procedure and, finally, prevention of side effects such as nausea, vomiting and seizures.[6] Sarang and Dinsmore[7] retrospectively examined 3 different anesthetic techniques: sedation with propofol, fentanyl, droperidol, and midazolam, second AAA with propofol infusion, and IV fentanyl with spontaneous ventilation via an LMA; and AAA anesthesia with propofol and remifentanil and intermittent positive pressure ventilation via an LMA. All these procedures guarantee reasonable patient comfort and satisfaction, but the deep sedation they produce, can jeopardize the benefits of the functional intraoperative testing.[7] In this study, the conscious sedation technique was used for awake craniotomy allowing the patient to breathe spontaneously without any tracheal or laryngeal device to protect their airway, minimizing sedation, and avoiding the use benzodiazepine. We think that a cooperative patient who does not feel pain is better than an over sedated or drowsy patient with unpredictable behavior, so the preoperative visit in our protocol is of utmost importance to explain the full details of the technique and to exclude patients that may not be cooperative.

Benzodiazepine administration could be criticized, as the effect on vigilance is unpredictable, and it could interfere with functional brain mapping. This is an issue of argument, Zorzi et al[17] considered it one of their routine drugs given preoperatively considering the interval elapse between benzodiazepine administration and electrophysiologic mapping of cortical areas (when the patient has to be awake) is at least 2 hours. We did not agree with this concept as the synergistic sedative effect of other drugs given to the patient such as clonidine, fentanyl, and propofol make the patients response unpredictable. We preferred to use the least amounts of drugs, depending mainly on propofol infusion. Propofol has certain characters including ease of titration, rapid and smooth recovery, antiemetic properties, it has a sedative effect that is more euphorigenic than neuroleptic in character, decreasing ICP, and a reduced incidence of intraoperative seizures

The mean duration of hospital stay was 3.8 ± 4.15 days in the awake group, while it was 8.15 ± 6.5 days in the GA group, only 2 cases needed ICU admission This is the main advantage of awake craniotomy: saving the resources of the hospital, the man power, reducing the potential for infection, and increased patient satisfaction. Blanshard et al[2] concluded that patients undergoing awake craniotomy can be discharged on the same or next day after surgery provided stringent criteria for patient selection are made.[22]

In this study, we found the incidence of neurological complications, ICU admission, and hospital stay statistically less in awake patients, but with a higher incidence of hypertension. Meanwhile, the incidence of tight brain, anesthetic complications, respiratory depression, airway obstruction, pain, nausea, vomiting, and seizure activity were acceptable and managed intraoperatively. None of our awake patients shifted to GA.

In conclusion, although awake craniotomy did not solve the dilemma of managing low-grade gliomas, compared to GA it allows safer tumor removal without any added deficit, especially in the immediate postoperative period. Awake craniotomy is a relatively simple procedure that does not require sophisticated technology to apply and that allows tumor removal guided by physiology rather than the anatomy. It is a relatively safe procedure with minimal morbidity, and we believe that it can be applied with any tumor other than gliomas as long as eloquent areas are concerned.

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